

CLAIMS

1. An antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 of any one of (1) - (12):

(1) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 123, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 124, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 125;

(2) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 109, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 110, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 111;

(3) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 106, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 107, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 108;

(4) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 132, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 133, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 134;

(5) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 106, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 135, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 136;

(6) CDR1 comprising the amino acid sequence set forth in SEQ

ID NO: 126, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 127, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 128;

(7) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 129, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 130, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 131;

(8) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 103, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 104, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 105;

(9) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 118, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 121, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 122;

(10) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 115, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 116, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 117;

(11) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 112, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 113, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 114; or

(12) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 118, CDR2 comprising the amino acid sequence set forth

in SEQ ID NO: 119, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 120.

2. An antibody comprising a light chain variable region having CDRs 1, 2 and 3 of any one of (1) - (13):

(1) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 143, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(2) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 143, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 145;

(3) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 140, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 141, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 142;

(4) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 167, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 168, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 169;

(5) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 170, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 171;

- (6) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 159, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 160, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 161;
- (7) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 162, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 147, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 163;
- (8) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 164, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 165, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 166;
- (9) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 137, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 138, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 139;
- (10) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 155, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 156, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 157;
- (11) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 149, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 150, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 151;
- (12) CDR1 comprising the amino acid sequence set forth in SEQ

ID NO: 146, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 147, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 148; or

(13) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 152, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 153, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 154.

3. An antibody selected from the group consisting of any one of (1) - (13):

(1) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 143, 144 and 158, respectively;

(2) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 109, 110 and 111, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 143, 144 and 145, respectively;

(3) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 106, 107 and 108, respectively, and a light

chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 140, 141 and 142, respectively;

(4) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 132, 133 and 134, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 167, 168 and 169, respectively;

(5) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 106, 135 and 136, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 170, 144 and 171, respectively;

(6) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 126, 127 and 128, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 159, 160 and 161, respectively;

(7) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 129, 130 and 131, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the

amino acid sequence set forth in SEQ ID NO: 162, 147 and 163, respectively;

(8) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 129, 130 and 131, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 164, 165 and 166, respectively;

(9) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 103, 104 and 105, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 137, 138 and 139, respectively;

(10) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 118, 121 and 122, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 155, 156 and 157, respectively;

(11) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 115, 116 and 117, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 149, 150 and 151,

respectively;

(12) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 112, 113 and 114, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 146, 147 and 148, respectively; and

(13) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 118, 119 and 120, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 152, 153 and 154, respectively.

4. An antibody having a heavy chain variable region of any one of (1) - (7):

(1) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 84;

(2) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 85;

(3) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 86;

(4) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 87;

(5) a heavy chain variable region comprising the amino acid

sequence set forth in SEQ ID NO: 88;

(6) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 89; or

(7) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 90.

5. An antibody having a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 92.

6. An antibody selected from the group consisting of the antibody of any one of (1) - (7):

(1) an antibody comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 84 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 92;

(2) an antibody comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 85 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 92;

(3) an antibody comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 86 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 92;

(4) an antibody comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 87

and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 92;

(5) an antibody comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 88 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 92;

(6) an antibody comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 89 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 92; and

(7) an antibody comprising a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 90 and a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 92.

7. An antibody having an activity equivalent to the activity of the antibody of any one of Claims 1-6, wherein one or more amino acid residues are substituted, deleted or added and/or inserted from the amino acid sequences set forth in any one of Claims 1-6.

8. The antibody as claimed in any one of Claims 1-7 which is a humanized antibody.

9. A humanized antibody capable of binding to glypican 3.

10. An antibody capable of binding to a peptide consisting of the sequence of the amino acid residues 524 - 563 of glypican 3.

11. An antibody capable of binding to a peptide consisting of the sequence of the amino acid residues 537 - 563 of glypican 3.

12. The antibody as claimed in Claim 10 or 11 which does not bind to a peptide consisting of the sequence of the amino acid residues 550 - 563 of glypican 3.

13. An antibody capable of binding to a peptide consisting of the sequence of the amino acid residues 544 - 553 of glypican 3.

14. An antibody capable of binding to a peptide consisting of the sequence of the amino acid residues 546 - 551 of glypican 3.

15. The antibody as claimed in any one of Claims 9-14 which is a humanized antibody.

16. An antibody capable of binding to an epitope to which

a second antibody is capable of binding, wherein said second antibody comprises a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 143, 144 and 158, respectively.

17. An antibody capable of binding to glypican 3 which has a high CDC activity against a cell expressing glypican 3.

18. An antibody capable of binding to glypican 3 which has a high ADCC activity against a cell expressing glypican 3.

19. A polynucleotide coding for a heavy chain variable region or a light chain variable region of the antibody as claimed in any one of Claims 1-18.

20. The polynucleotide as claimed in Claim 18 having the sequence set forth in SEQ ID NOs: 11-21, 33-43, 55-59, 65-70 and 77-83.

21. A cell-growth inhibitor comprising as an active ingredient the antibody as claimed in any one of Claims 1-18.

22. An anticancer agent comprising as an active ingredient the antibody as claimed in any one of Claims 1-18.

23. The anticancer agent as claimed in Claim 22 for treatment of hepatoma.

24. A peptide comprising the amino acid sequence of the amino acid residues 524 - 563 of glypican 3.

25. A peptide comprising the amino acid sequence of the amino acid residues 537 - 563 of glypican 3.

26. A peptide comprising the amino acid sequence of the amino acid residues 544 - 553 of glypican 3.

27. A peptide comprising the amino acid sequence of the amino acid residues 546 - 551 of glypican 3.

28. An antibody comprising a light chain variable region having CDRs 1, 2 and 3 of any one of (1) - (15):

(1) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 174, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(2) CDR1 comprising the amino acid sequence set forth in SEQ

ID NO: 175, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(3) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 176, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(4) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 177, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(5) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 178, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(6) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 179, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(7) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 180, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(8) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 181, CDR2 comprising the amino acid sequence set forth

in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(9) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 182, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(10) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 183, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(11) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 184, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(12) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 185, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(13) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 186, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158;

(14) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 187, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence

set forth in SEQ ID NO: 158;

(15) CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 188, CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 144, and CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 158.

29. An antibody selected from the group consisting of the antibody of (1) - (15):

(1) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 174, 144 and 158, respectively;

(2) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 175, 144 and 158, respectively;

(3) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 176, 144 and 158,

respectively;

(4) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 177, 144 and 158, respectively;

(5) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 178, 144 and 158, respectively;

(6) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 179, 144 and 158, respectively;

(7) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 180, 144 and 158, respectively;

(8) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 181, 144 and 158, respectively;

(9) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 182, 144 and 158, respectively;

(10) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 183, 144 and 158, respectively;

(11) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 184, 144 and 158, respectively;

(12) an antibody comprising a heavy chain variable region

having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124, and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 185, 144, and 158, respectively;

(13) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124, and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 186, 144 and 158, respectively;

(14) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 187, 144 and 158, respectively; and

(15) an antibody comprising a heavy chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 123, 124 and 125, respectively, and a light chain variable region having CDRs 1, 2 and 3 comprising the amino acid sequence set forth in SEQ ID NO: 188, 144 and 158, respectively.

30. An antibody having a light chain variable region selected

from (1) - (15):

- (1) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 191;
- (2) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 192;
- (3) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 193;
- (4) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 194;
- (5) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 195;
- (6) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 196;
- (7) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 197;
- (8) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 198;
- (9) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 199;
- (10) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 200;
- (11) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 201;
- (12) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 202;

- (13) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 203;
- (14) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 204; and
- (15) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 205.

31. An antibody having a light chain variable region selected from the group consisting of (1) - (15):

- (1) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 191;
- (2) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 192;
- (3) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 193;
- (4) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 194;
- (5) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 195;
- (6) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 196;
- (7) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 197;
- (8) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 198;

- (9) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 199;
 - (10) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 200;
 - (11) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 201;
 - (12) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 202;
 - (13) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 203;
 - (14) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 204; and
 - (15) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 205;
- and a heavy chain variable region selected from the group consisting of (1) - (7):
- (1) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 84;
 - (2) a heavy chain variable region comprising; the amino acid sequence set forth in SEQ ID NO: 85;
 - (3) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 86;
 - (4) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 87;
 - (5) a heavy chain variable region comprising the amino acid

sequence set forth in SEQ ID NO: 88;

(6) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 89; and

(7) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 90.

32. The antibody as claimed in any one of Claims 28 - 31 which is a human antibody.